VITAMIN B_1 AND CARBOHYDRATE METABOLISM (IN THE DOG)

by

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A relationship between vitamin B_1 and carbohydrate metabolism has been indicated by the findings of many investigators. This report will not attempt an exhaustive review of the literature since this is available in recent monographs on vitamins (Sherman and Smith, 1931; Browning, 1931; Medical Research Council, 1932; Cowgill, 1934). However, mention of the findings of a few will serve to show cause for our interest in the present problem and furnish a background for the work to be presented.

Blood sugar. Several authors have claimed a vitamin B deficiency leads to a hyperglycemia. Collazo (1923) found that deprivation of B caused first a fall then a rise in blood sugar. A similar hyperglycemia was found in starving animals. Stucky and Rose (1929) found that the blood sugar level in B deficient dogs remained normal. V. Drigalski (1936) obtained no alteration in the blood sugar level by feeding yeast. Likewise the extract used by Mills (1928) was without effect upon the normal fasting blood sugar level. On the other hand, Bickel (1926) and Kauffmann-Costa, Vasiloo and Ceriu (1932) found the C/N ratio in the urine invariably increased in vitamin B deficient animals. They termed such disturbance of carbohydrate metabolism "dysoxydative carbonuria."

Liver glycogen. Eggleton and Cross (1925) using rats showed that as the animal becomes depleted of vitamin B the liver glycogen falls. Mills (1926) fed an extract rich in vitamin B to rabbits and found that such animals had considerably more glycogen in the liver than normal controls. Bickel and Wigmann (1929) by feeding dried yeast to rabbits starved forty-eight hours demonstrated an increase in liver glycogen in these animals over controls. It was the conclusion of Labbe, Nepveux and Gringoire (1933) that vitamin B favors glycogen formation of the liver. Contrary to above findings Abderhalden (1932) reported that pigeons fed on a B deficient diet showed an increase (6.3%) in liver glycogen.

Amount of carbohydrate fed. Cowgill (1934) states, "It is quite generally agreed that the characteristic symptoms of vitamin B_1 deficiency do not appear as readily in animals subjected to complete starvation as in those who eat appreciable amounts of the ration deficient in this dietary essential. From this point of view the loss of appetite for the B_1 deficient diet may be regarded as a reaction protecting the animal against development of an unfortunate syndrome." Thus it is concluded that vitamin B_1 plays a role in carbohydrate metabolism since the greater the intake of carbohydrate the more vitamin B is needed to protect the animal.

Dextrose tolerance. Lepkovsky, Wood and Evans (1930) studied the dextrose tolerance of vitamin B_1 deficient rats and found it unchanged until late in deficiency. Only when their rats approached a final breakdown from beri beri did the glucose tolerance become poor. Eggleton

and Cross (1926) had made a similar finding using rats and killing at different time intervals. Their deficient rats had a little higher blood sugar level but the composite tolerance curve was practically identical with that of normals. Kauffmann-Costa, Vasilco and Ceriu (1932) made observations on sugar tolerance of dogs on a standard diet with vitamin B_1 and when B_1 was withheld. Glucose was given by stomach tube and the amount of glucose found in the twenty-four hour specimen of urine used as a criterion. While B_1 deficient animals in the course of three weeks showed more glucose in the urine upon administration of glucose by mouth there is no mention as to the dogs' appetite. They must have assumed all food was eaten but we know that this will not happen when the animal becomes depleted. He eats less or refuses food. His tolerance is of course now much less because of the fact that his intake is less. The work of Burack and Cowgill (1932) is a good illustration of this last point but unfortunately is not of much value in determining the relation of vitamin B_1. These authors undertook to show a possible relationship of B to carbohydrate metabolism by carrying a control dog that received vitamin B_1 and only as much food as the B deficient dog ate. Thus both animals were affected by inanition and any influence that B might have was complicated by the effect of inanition.

Absorption rate. Eggleton and Cross (1925) concluded that the rate of absorption in rats is unaffected by a vitamin B_1 deficiency. These findings were confirmed by Pierce, Osgood and Polansky (1926). However, Gal (1930) found that the emptying time of the stomach in rats with B_1 deficiency was prolonged and absorption slower than in normals. If

Gal's finding is correct sugar tolerance curves in B_1 deficiency may not be a true index when the sugar is given by mouth because of delayed absorption.

In reviewing the above findings with regard to carbohydrate metabolism it seems to us that lack of agreement among various investigators lies in the fact that a clear distinction has not been made between a vitamin B_1 deficiency and that deficiency complicated by inanition. Since beri beri actually comes on long after the appetite has fallen off and thus after general nutrition is disturbed, it seems that disturbances in carbohydrate metabolism may be studied early, that is before complicated by inanition.

Diabetes Mellitus. Yeast and vitamin B have been used in the treatment of diabetes in man with varying results. Wills (1926) used an extract made from plants known to be rich in vitamin B. This extract had no effect on depancreatised dogs but lowered the hyperglycemia in severe cases of diabetes mellitus when given orally. Labbe, Nepveux and Gringoire (1933) obtained a fall in urine sugar and a rise in carbohydrate tolerance in eight of eleven diabetic individuals upon administration of a vegetable powder rich in vitamin B. Von Drigalski early in 1935 reported his observations made upon ten diabetics that vitamin B (yeast) has no influence upon sugar excretion, acidosis, blood sugar level, insulin need, body weight and course of the disease. Vorhaus, Williams and Waterman (1936) made a careful study of the effects of crystalline B_1 in diabetes. They state, "In a series of eleven cases of proven diabetes mellitus (according to present day standard) to whom an average of ten mgms. of vitamin B_1 were

administered daily for twenty-eight consecutive days, six (or 54.6%) showed an increased carbohydrate utilization. Five cases (45.5%) showed no increase. Two of the six positive cases lost the gain in carbohydrate utilization as soon as the administration of vitamin B_1 was stopped. In four cases, the increase continued for periods ranging from two to ten months. Two of these four are still maintaining the gain."

Liver Fat. McHenry (1936) observed the effect of crystalline vitamin B_1 in minute doses upon liver fat. Forty-eight young male or female rats were divided into two equal groups, one receiving the basal diet only, the other the basal diet and vitamin B_1. Those rats receiving the basal diet showed an average of 9.23% liver fat; while those receiving the basal diet and vitamin B_1 showed an average of 17.03% liver fat. The basal diet used was very low in choline content. It was shown that the presence of choline decreased the amount of fat in the liver. If choline were given in amounts of 5 mg. per day along with B the action of B to increase the liver fat was absent. The results of this experiment were of interest to us, for it was thought that vitamin B_1 might aid in the prevention of fatty degeneration and infiltration of the liver which occurs in the completely depancreatized dog that receives insulin without raw pancreas added to the diet. Dogs receiving no raw pancreas usually died within two to five months. However, Chaikoff (1936) reports that the completely depancreatized dog can survive for well over four years when maintained with insulin and a diet containing meat, sucrose, bone ash and vitamin supplements, B (in the form of rice bran concentrate), and A and D (as cod liver oil). No other accessory substances were found essential. These animals were not normal. They developed

cataracts. The blood lipids fell in concentration with a rise in the lipid content of the liver. It was then shown that the addition of raw pancreas to the diet decreased the lipid content of the liver to normal levels and caused a rise in blood lipids to values far in excess of the pre-operative normal level. The maintenance of a high blood lipid level was observed only so long as raw pancreas was being ingested. When this glandular tissue was withheld from the diet an abrupt fall in the lipid level occurred.

The effect of diet on liver fat has been shown by a number of workers. Channon and Wilkinson (1935) have shown that the amount of fat in the livers of rats was controlled by the amount of protein in the diet. The protein was supplied in the form of caseinogen, the amount varied from 5% to 50% of the diet at the expense of the carbohydrate. A constant fat content (40%) was maintained. Adequate vitamins and salts were supplied. Later, Beeston, Channon and others studied again the effects of dietary caseinogen on liver fat of rats. They have expressed the amount of casein required to present liver fat deposition in terms of a standard, that is in mg. of choline. They found that 1 gram of casein is equivalent in its preventative action on liver fat deposition to 7 - 8 mg. of choline. Further it was shown that marmite (vitamin B), the presence or absence from the diet, had no influence on liver fat accumulation than that anticipated from its choline content. 100 grams of marmite contains 440 mg. of choline. Caseinogen contains only .6 mg. of choline per 100 grams of caseinogen. In preventative experiments on diets containing 5% caseinogen and 40% of fat and 3 mg. of choline per rat per day caused reduction of liver fat

from 20% to 10%. Choline in amounts varying from 6.8 to 79.6 mg. per day did not prevent some fat accumulation in the liver.

Our dogs were fed on a diet containing 41.2% of casein. This should certainly prevent the dietary production of fatty livers in the normal animal. However, our completely depancreatized dogs, which did not receive raw pancreas, showed marked fatty livers at autopsy.

Procedure:

The following procedure was designed to permit a study of the relationship between carbohydrate metabolism and vitamin B_1.

All of the dogs used in this work were placed on a standard diet described by Cowgill (1924) with a salt mixture used by Karr (1920). It contained the following:

	Gms.	Per cent
Casein (Harris)	6.3	41.2
Sucrose	4.5	29.4
Lard	2.8	18.3
Butter	1.1	7.2
Bone ash	.4	2.6
Salt mixture	.2	1.3
	15.3	100.0

This diet allows 73 calories per kilo body weight which in some of our dogs was more than needed to maintain body weight.

Series 1.

Ten normal dogs were placed on the standard diet and ample vitamin B_1 and then subjected to glucose tolerance tests. These tests were repeated with the dogs on the standard diet without vitamin B_1.

Glucose was given per os in most of the experiments but in some it was given intravenously to check upon the possible effect of delayed absorption and reduced motility of the gastro-intestinal tract which possibilities may occur in late vitamin B_1 deficiency.

Series 2.

Eight partially depancreatised dogs were used following the same procedure as outlined under series 1.

In the first and second series the dogs were fed once a day at a regular hour and water was allowed ad libidum. Glucose tolerance tests were run 15 to 20 hours after feeding at intervals of 5 to 7 days. Thus the glucose given could not complicate the next tolerance curve. The amount of glucose given was one gram per kilo of body weight in 25% solution by stomach tube. Blood samples were drawn from the femoral or saphenous vein 15, 30, 60, and 120 minutes after glucose administration. When given intravenously, one half gram of glucose per kilo body weight was injected into the saphenous or femoral vein in 50% solution. Blood samples were drawn at 6, 16, 26, 36, 46, 60, 80, 100 and 120 minutes after injection.

Series 3.

Two completely depancreatised dogs were used in this series. Following pancreatectomy these animals were placed on the standard diet and the amount of insulin injected subcutaneously was adjusted to the needs of the animal. The dogs were fed twice a day. Dog I received 87 grams of food or one-half of the total calculated diet at 8:00 a.m.

and 5 units of insulin. At 4:00 p.m. the dog received 87 grams of food and 5 units of insulin. Dog 2 received 95 grams of food and 15 units of insulin at 8:00 a.m. and 4:00 p.m. The time of feeding and insulin dosage were not varied. The results are not complicated by failure of the dogs to eat the diet. The only variable quantity was the addition or subtraction of vitamin B to the standard diet. Fasting blood sugars, urine volumes, and grams of sugar in the urine were followed daily.

A further check on these animals was run in the following manner. The food and insulin given as described above at 8:00 a.m. and 4:00 p.m. served as "test meal tolerances". A fasting blood sample was obtained before the food and insulin were given. Then blood samples were taken at 11 a.m., 2 p.m. and 4 p.m. (just before the afternoon feeding). Blood samples were then taken at 7 p.m., 10 p.m. and 12 p.m. By this means we were able to follow the blood sugar after food ingestion and insulin injection. Later the "test meal tolerance" was limited to that following the 8 a.m. feeding and insulin injection. It was found that after the 4 p.m. feeding and insulin injection a duplication of the morning tolerance occurred. Furthermore, it reduced the amount of blood withdrawn from the animals. It is necessary to state that the food was immediately eaten when given to these animals.

Methods.

Blood sugar and urine sugar determinations were made using the Hanogyi modification of the Schaffer-Hartmann method (1933). The

blood filtrates were prepared by the ferric sulphate, barium carbonate precipitation method as described by Steiner, Urban and West (1932). Urine filtrates were prepared by the ferric sulphate barium carbonate, Lloyd's reagent precipitation method as described by West, Lamb and Curtis (1935).

Vitamin B_1 was supplied in pulvule form as prepared by Eli Lilly and Company. Each pulvule contains approximately 200 Sherman units.

Results on series 1.

Figures 1, dogs 1, 2, 3, 4, are shown to illustrate types of tolerance curves that may be obtained from normal dogs on the standard diet and one pulvule of vitamin B_1 administered daily. They are all composite curves - the result of many tests after glucose administration per os. They agree in that the peak is reached in 30 minutes and a return to original blood sugar level is reached in approximately 90 minutes. There is a wide difference in range of peak and general shape of curve. Under laboratory conditions for three months these animals remained in good condition which assured us concerning the adequacy of the diet. However, when these animals were finally placed on a B_1 deficient diet, they failed to consume the diet regularly and the results were accordingly complicated by inanition. These results had to be discarded. The results on dogs 5, 7, and 8 were likewise complicated by failure of the animals to eat the diet regularly and had to be discarded.

Figures 1, 3, 4, and 5, dog 6, represent a series of observations under different conditions. In figure 1, the animal's normal responses are shown after dextrose by stomach. It will be noted that this dog normally showed a maximal blood sugar at 15 minutes. During this time the dog was receiving one pulvule of vitamin B_1 daily. In figure 2, after 9 days without B a normal response is shown, but on the 16 day of B deficiency the curve is materially drawn out. Five days after the last curve the dog refused to eat the diet. One pulvule of vitamin B_1 was added to the diet daily until appetite was restored. The animal was again placed on the B deficient diet. This deficiency period is represented by the curves in figure 4. The 6 day curve is not normal, and the 17 day curve shows a marked alteration in response. Shortly after this time the dog developed anorexia and the appetite was restored by the addition of one pulvule of vitamin B_1 to the diet. The vitamin was again withheld, and the results are shown in figure 5 after 10, 15, and 22 days of B_1 deficiency. The tendency to show a delayed return to normal is again evidenced.

Figures 1, dogs 8 and 9 represent the results when intravenous tolerance tests were taken on normal and B deficient animals. The curves marked "a" represent a composite of two tests during the time the animals were receiving the standard diet and one pulvule of vitamin B_1 daily. Curves marked "b" represent the average of our tests 5, 11, 18 and 24 days after vitamin B_1 was removed from the diet. Here is seen a distinct tendency to lowered carbohydrate tolerance not open to criticism on the basis of delayed absorption.

Results on series 2.

Of the eight dogs used in this series, only the results of three animals are reported. Dogs 1, 2, 3, 4, and 6 failed to regularly consume the standard diet over a period of time.

In figure 1, dog 7, three curves are represented. The first curve 20 days, the second curve 37 days and the third curve 67 days after the administration of two pulvules of vitamin B_1 daily with the standard diet. In figure 2, the curves represent the tolerance tests taken 10, 16, 20 and 25 days after vitamin B_1 was withheld from the diet. The 20 and 25 day curves differ from the curves obtained when the dog was receiving vitamin B_1 in that the initial rise of blood sugar occurred more rapidly and that the blood sugar tends to reach higher levels at the 60 minute interval.

In figure 1, dog 8, the solid line represents the animal's type of response when receiving one pulvule of vitamin B_1 daily with the standard diet. The broken line is constructed from three tests in a 16 day period of avitaminosis B_1 and shows only a delayed peak in comparison to the former.

In figure 2, dogs 4a and 7a, the results of intravenous glucose tolerance tests are given. In figure 1, dog 4a, the 12 and 18 day curves during vitamin B_1 deficiency are markedly altered in comparison to the curve obtained during B administration. In figure 1, dog 7a, this marked altering of tolerance during the period of avitaminosis B_1 is lacking.

The amount of pancreas removed in these animals was as follows. Dog 7 (Va), approximately three-fourths, dog 46, approximately four-fifths, and dog 5 approximately three-fourths of the pancreas was removed.

Results on series 3.

Two dogs were used in this series. The results obtained were difficult to interpret in regard to the relation of vitamin B_1 to the diabetic condition. The complete removal of the pancreas causes fatty infiltration and degeneration of the liver. Raw pancreas was not fed to these dogs for we desired to find out if vitamin B_1 might aid in the prevention of such liver changes.

In figure 1, dog, 1, three curves are represented following a "test meal tolerance" as explained in the procedure. Blood samples were taken at 8 a.m., (fasting), 2 p.m. and 4 p.m. The first curve was run 2 months and 15 days after pancreatectomy; the second curve 2 months 21 days, and the third curve 3 months 5 days after pancreatectomy. During the intervals between the curves, fasting blood sugar and urine sugar determinations were made.

It is seen that only in the first curve is there a rise of blood sugar after the maximum effect of insulin which occurred at 11 a.m.

In the second curve there is no rise of blood sugar after 11 a.m., but a continual slow drop until 4 p.m.

In the third curve the fasting blood sugar is extremely low. In the interval between this curve and the second curve the animal had been regularly receiving 95 grams of food at 8 a.m. and 5 units of insulin, and 95 gramm of food and 5 units of insulin at 4 p.m. The curve is not

complicated by failure of the animal to consume the diet. In this interval, the fasting blood sugar determinations revealed a gradual lowering of the blood sugar level to amounts that varied between 54 to 76 mg. per 100 cc. of blood. This means that 16 hours after the afternoon feeding and insulin, the blood sugar failed to return to the high levels of the fasting blood sugars obtained during the second month following pancreatectomy. This 16 hour period following food and insulin administration speaks for an adequate length of time for stomach emptying and intestinal absorption. In curve number 3, then, the low fasting blood sugar is in accordance with the previous fasting blood sugars obtained. It is seen that from 8 a.m. to 11 a.m. there is a rise of blood sugar, and from 11 a.m. to 2 p.m. a lowering. From 2 p.m. to 4 p.m. there occurs a slight gradual rise. This latter curve shows that between 8 a.m. and 11 a.m. the food ingested at 8 a.m. probably was being absorbed. Thus in the latter two curves it is unlikely that the increased lowering of the blood sugar over an eight hour period was due to failure of food absorption from the intestinal tract. These curves show a progressive increased sensitivity of the animal to insulin over a period of time.

In figure 2, dog. 2 four curves are represented. The first curve shows a "test meal tolerance" 1 month after pancreatectomy and an avitaminosis B_1 for 11 days. The maximum effect of insulin occurred at 11 a.m. with a return of high blood sugar at 2p.m. and 4 p.m.

The second curve represents a "test meal tolerance" 1 month 7 days after pancreatectomy and 6 days after administration of 4 pulvules of vitamin B_1 daily. It is seen that very little difference between the

two curves exists.

The third curve represents a "test meal tolerance" 1 month 14 days after pancreatectomy with administration of vitamin B_1 daily (4 pulvules) for 12 days. In this curve the maximum effect of insulin occurs at 2 p.m. with marked retardation of the returning hyperglycemia characteristic of the previous two curves.

The fourth curve shows a tolerance two months after pancreatectomy and an avitaminosis B_1 of 12 days' duration. It is seen that the maximum effect of insulin occurs at 2 p.m. with a retardation of the returning hyperglycemia as noted in the third curve when ample B was being given.

Thus an increased sensitivity to insulin is demonstrated over a period of time. Vitamin B_1 did not alter this increased sensitivity, that is, in the third curve after 12 days of ample vitamin B_1 the rather rapid return of hyperglycemia noted in the first two curves did not appear, which might be expected if vitamin B_1 had any influence on restoring the animal to a certain physiological condition as that found in curves obtained one month after pancreatectomy. It must be granted, however, that vitamin B_1 was administered over an adequate length of time.

Discussion:

It is again to be noted that the above experimental work reported is not complicated by inanition. Only the results obtained during the period the animal was regularly consuming its calculated diet with or without vitamin B_1 are reported. The dextrose tolerance tests are therefore not complicated by failure of the animal to eat the diet. It is for this reason that the results presented are limited. A possible criticism arises that the number of animals used is inadequate to substantiate the following interpretation. An adequate number of animals were used, but complicated results occurred for the unknown reason that a certain number of the animals would not regularly consume the diet. Thus these animals had to be discarded. It was our aim, as far as the procedure was concerned, to hold the only variable to the addition or subtraction of vitamin B_1 to the calculated diet for the particularly animal concerned.

The results reported, then, in the normal group are from three animals. Figures 1 to 5, dog 6, are the results of dextrose tolerance tests after the administration of glucose by mouth with and without B_1. Figure 1, dogs 8 and 9 are the results of intravenous tolerance tests on two animals with and without B_1. While this group shows a definite tendency to a lowered sugar tolerance in vitamin B_1 deficiency, the results are not striking. The fact remains, however, that in these animals we have no other way of explaining this alteration in sugar tolerance except the lack of vitamin B_1.

Murdock and Cowgill (1932) accepted the decreased tolerance due to inanition and tried to superimpose the effects of lack of vitamin B_1. In the normal animal at least we feel that any effects of B deficiency may be readily obscured by such procedure.

In the partially depancreatised animals, the results of dextrose tests are reported on two dogs after dextrose by mouth and two dogs after intravenous dextrose. The results obtained from these animals are difficult to interpret due to the rather erratic responses on the part of the animal to handle a given amount of dextrose. In this respect, however, they resemble the diabetic individual. While there are differences in the curves of the two animals that received dextrose by mouth during avitaminosis B_1, the differences are not of such degree to warrant conclusions. This decision is particularly brought to attention by the curves obtained from the two dogs that received dextrose by vein. The curve obtained on the 18 day of B deficiency in figure 1, dog 7a, showed practically the same tolerance as that obtained during vitamin B_1 administration. The other animal, figure 1, dog 4a, showed a markedly decreased tolerance on the 12 and 18 day of B deficiency. Furthermore, there were slight differences in the amount of pancreas removed from these animals.

In the completely depancreatised animal, the results obtained from "test meal tolerance" curves on two dogs are shown. Figure 1, dog 1, demonstrates an apparent increased sensitivity to insulin over a period of time. The effect of vitamin B_1 in this animal is not shown owing to lack of complete data. However, in figure 1, dog 2, the results obtained

tend to show that vitamin B_1 has no effect on the progressive increased sensitivity to insulin which occurs in depancreatised dogs that do not receive fresh pancreas. This apparent increased sensitivity of the animals to insulin has been interpreted by Hershey and Soskin as failure of liver function, the liver losing its ability to form sugar (1931). These investigators report the return of increased tolerance for insulin, increased volume of urine and increased urine sugar in such animals after the administration of "lecithin". If vitamin B_1 acted in any beneficial manner in regard to liver cell function it would be expected that an increased tolerance to insulin should occur. Soskin found that "lecithin" caused a disapponrance of the fatty infiltration and degeneration of the liver which takes place as soon as six weeks after pancreatectomy. Evidence is given in the investigation of Hershey and Soskin that vitamins do not play any major role in the development or alleviation of this condition. Vitamin B was supplied to their animals in the form of brewer's yeast and "marmite". Our results in depancreatised dogs agree with the results of the above investigators that vitamin B does not aid in the prevention of such changes. The livers of these animals reported by us showed marked fatty infiltration and degeneration.

It is known that raw pancreas fed to such animals prevents these liver changes. Best and Huntsman (1932) suggested choline as the active substance in raw pancreas which prevents such changes, while Dragstedt, Prehskin and Harms (1936) isolated a substance from beef pancreas which they call "lipocaic" which prevents fatty infiltration and degeneration of the livers of depancreatised dogs. It is our opinion that even with the administration of raw pancreas or the other above named substances to our dogs, vitamin B_1 would be without effect in regard to the control of the diabetic condition.

SUMMARY

Normal and partially depancreatized dogs have been used to study the effects of vitamin B_1 deficiency on glucose tolerance. Blood sugar curves made after administration of glucose by stomach have been checked by intravenous administration of glucose. In the normal animals there is a tendency for decreased tolerance to occur in B_1 deficiency uncomplicated by inanition. In the group of partially depancreatized animals the results obtained do not indicate that B_1 played a significant role.

In the two completely depancreatized dogs in which the fatty degeneration and infiltration of the liver was not controlled, the possibility of the substitution of vitamin B_1 for insulin, in part or in whole, in the control of the diabetic condition, was not demonstrated.

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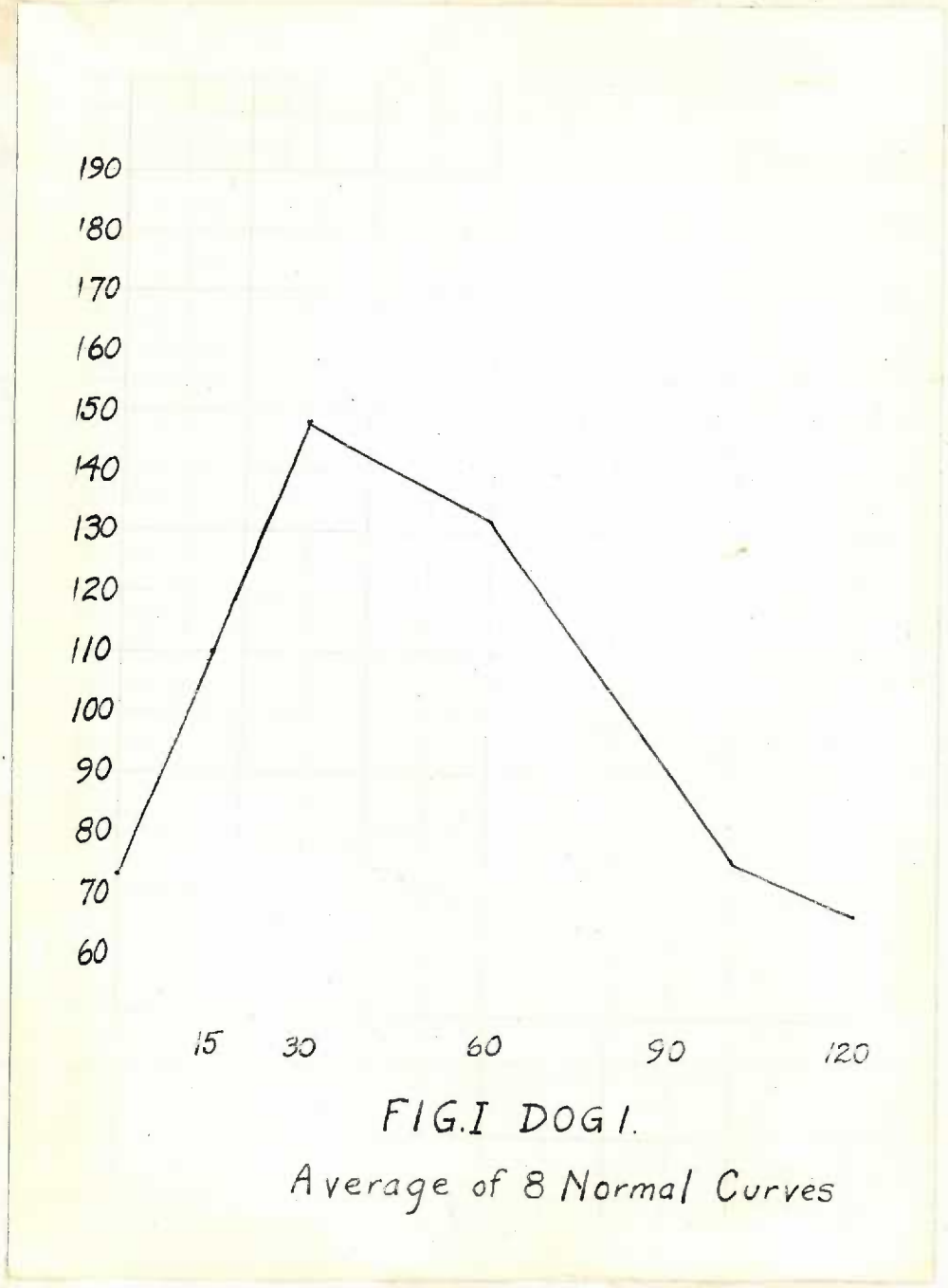

Fig. 1, Dog 1. Normal dog on standard diet and vitamin B. Composite curve of eight dextrose tolerance tests.

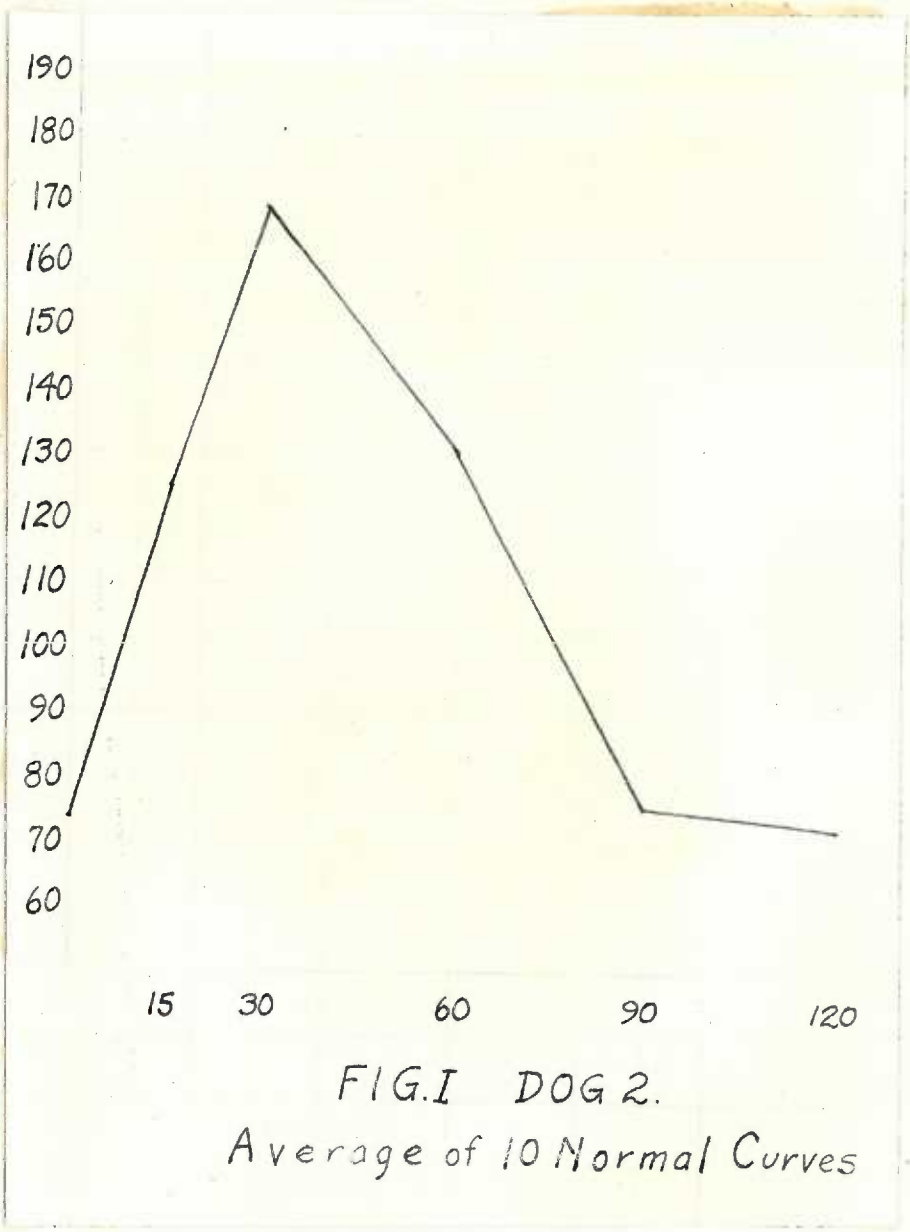

Fig. 1. Dog 2. Normal dog on standard diet and vitamin B. Composite curve of ten dextrose tolerance tests.

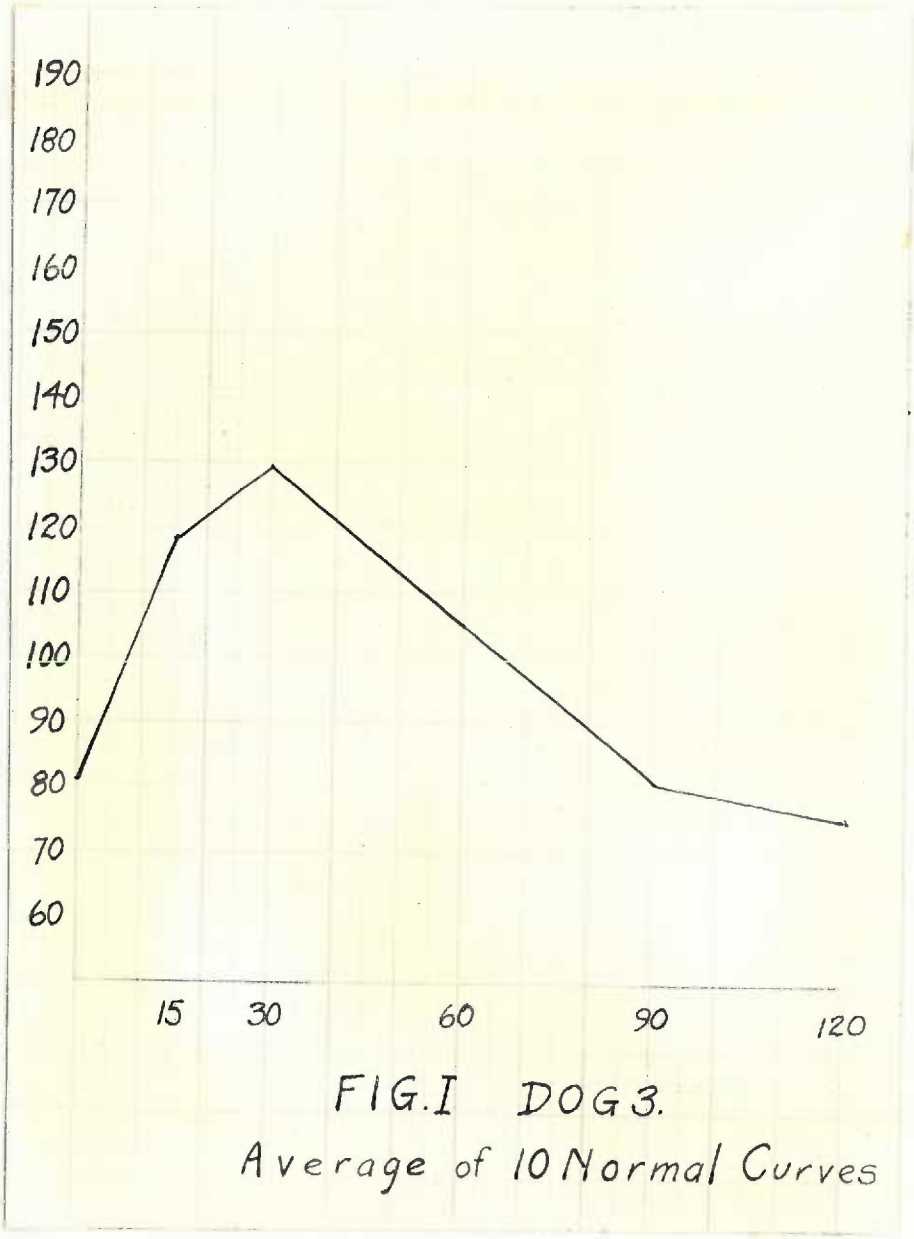

Fig. 1. Dog 3. Normal dog on standard diet and vitamin B. Composite curve of ten dextrose tolerance tests.

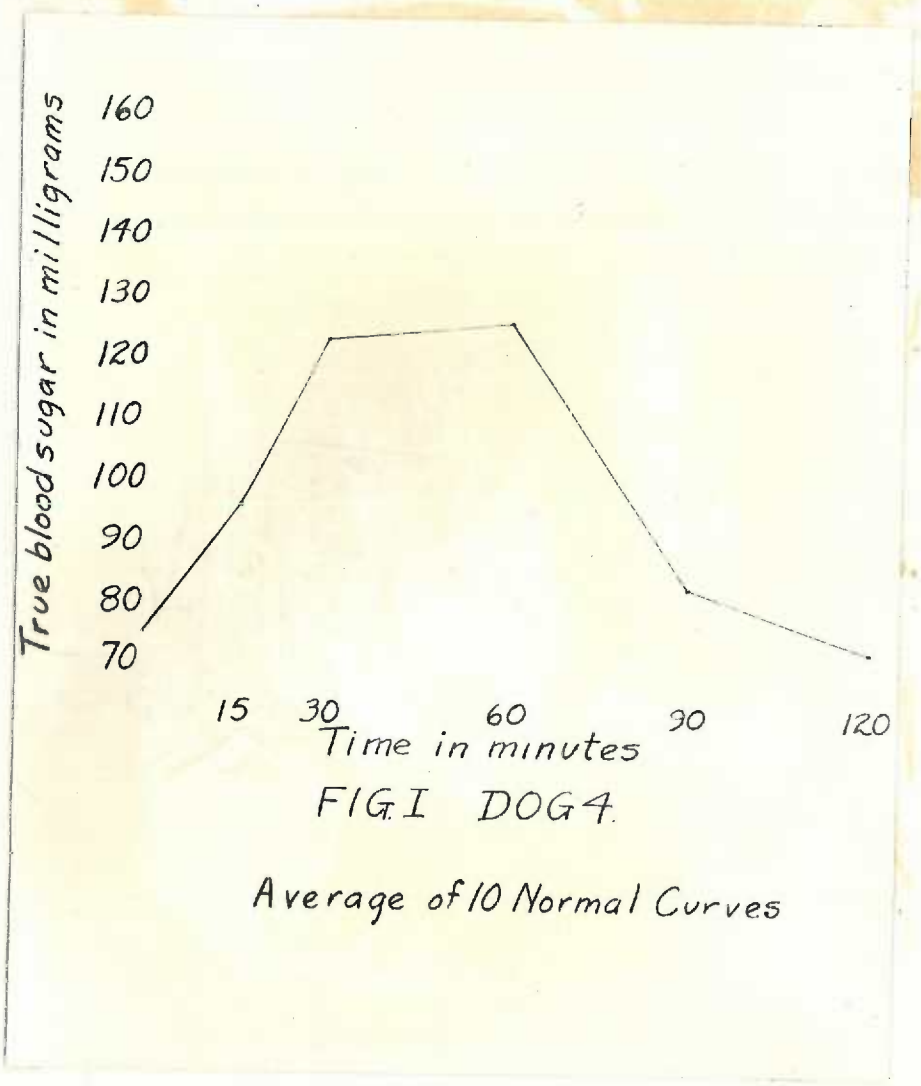

Fig. 1. Dog 4. Normal dog on standard diet and vitamin B. Composite curve of ten dextrose tolerance tests.

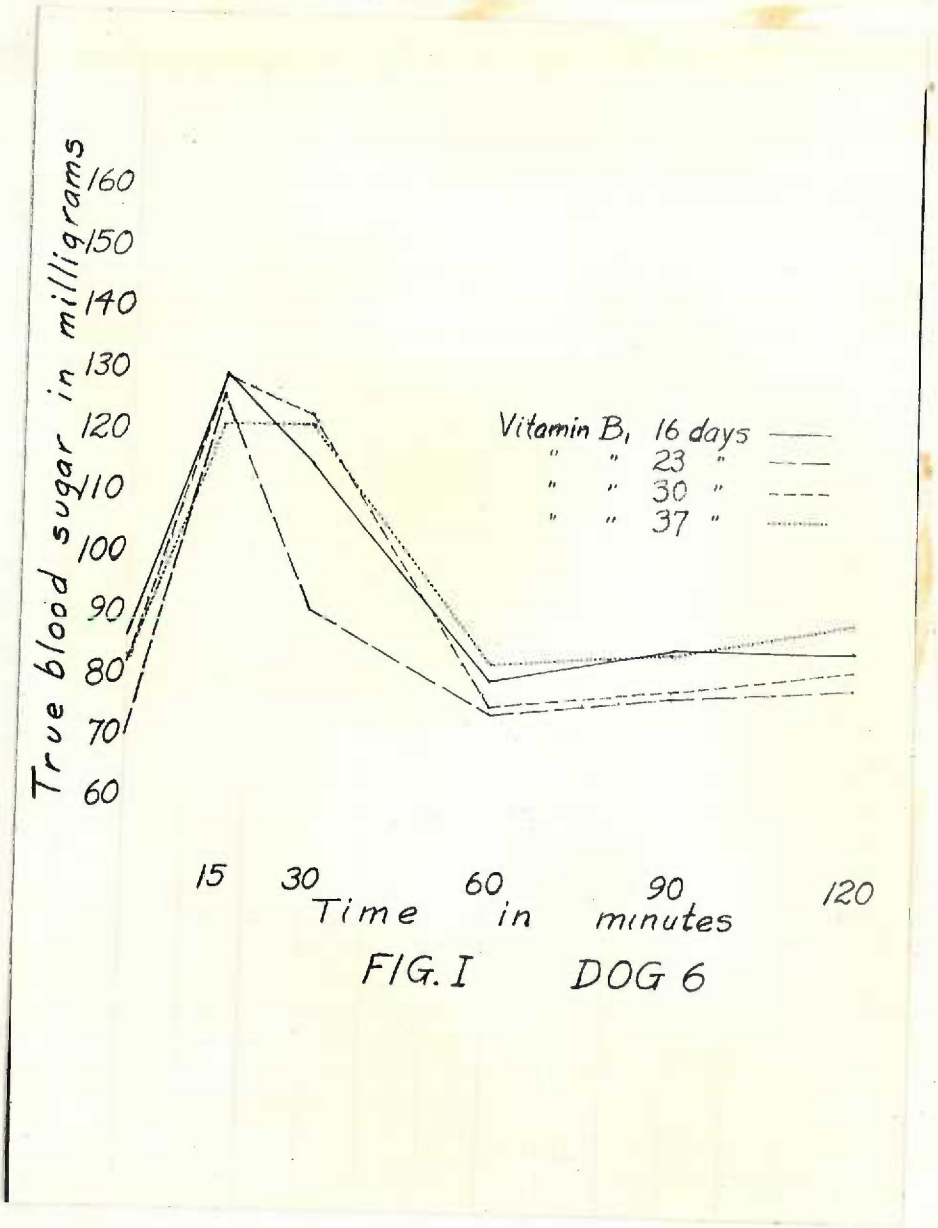

FIG. I DOG 6

Fig. 1, Dog 6. Dextrose tolerance tests on a normal dog 16, 23, 30, and 37 days after daily administration of one pulvule of vitamin B to the standard diet.

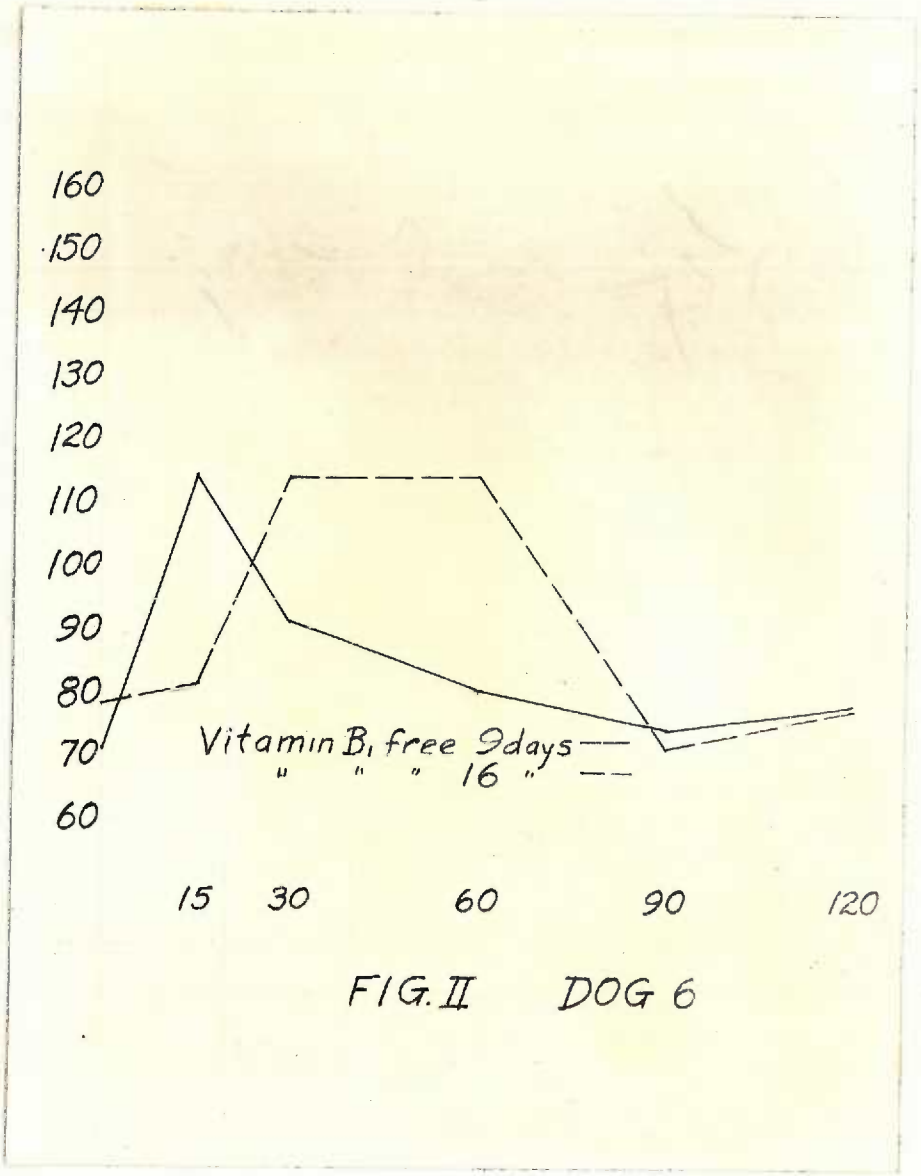

FIG. II DOG 6

Fig. 2. Dog 6. Normal dog on B deficient diet. Curves represent tolerance tests on the ninth and sixteenth day of B deficiency.

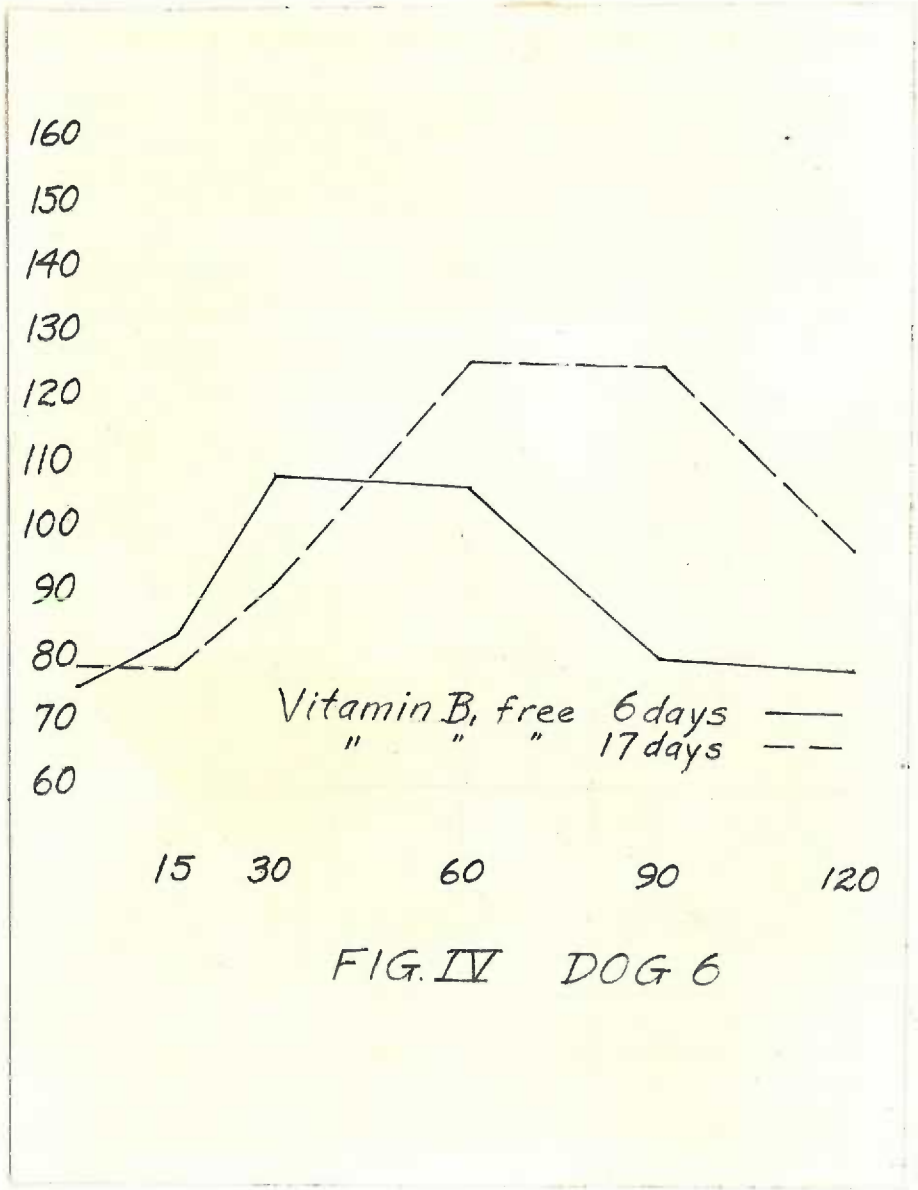

Fig. 4. Dog 6. Normal dog on B deficient diet. Curves represent tolerance tests on the sixth and seventeenth day of B deficiency.

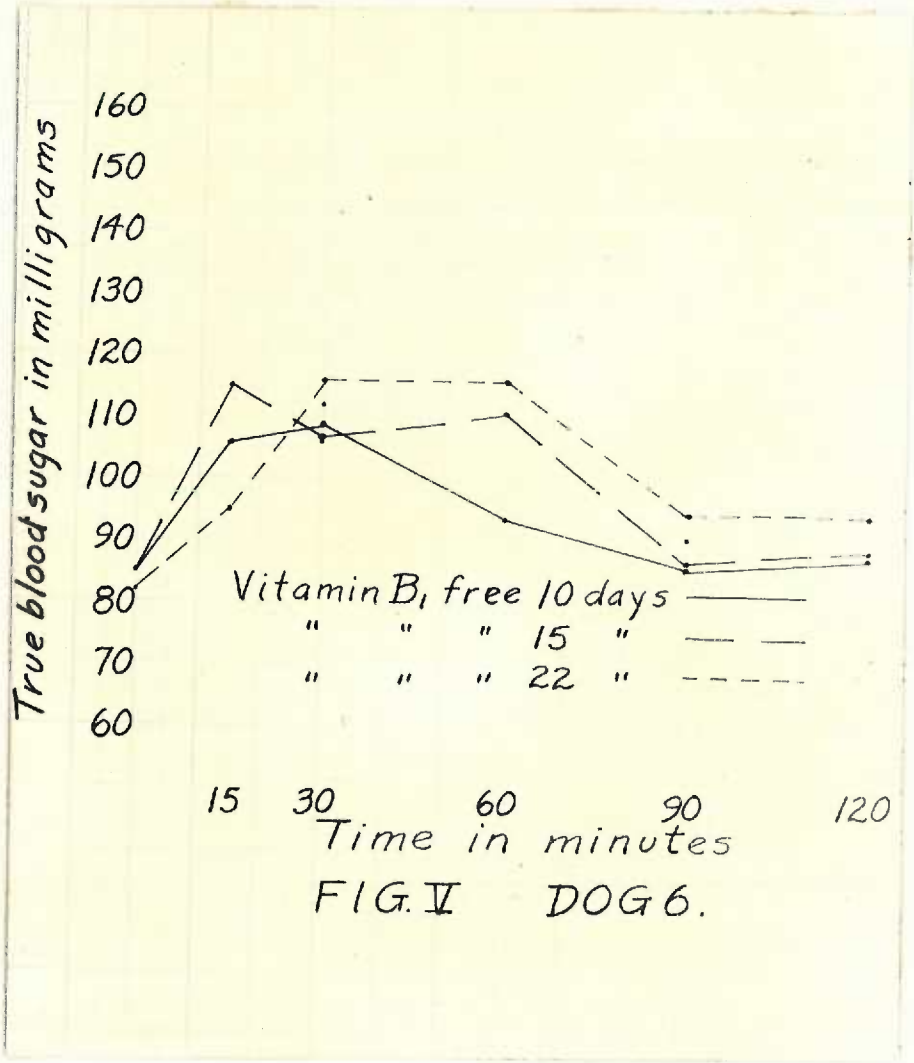

FIG. V DOG 6.

Fig. 5. Dog 6. Normal dog on B deficient diet. Curves represent tolerance tests on the tenth, fifteenth and twenty-second day of B deficiency.

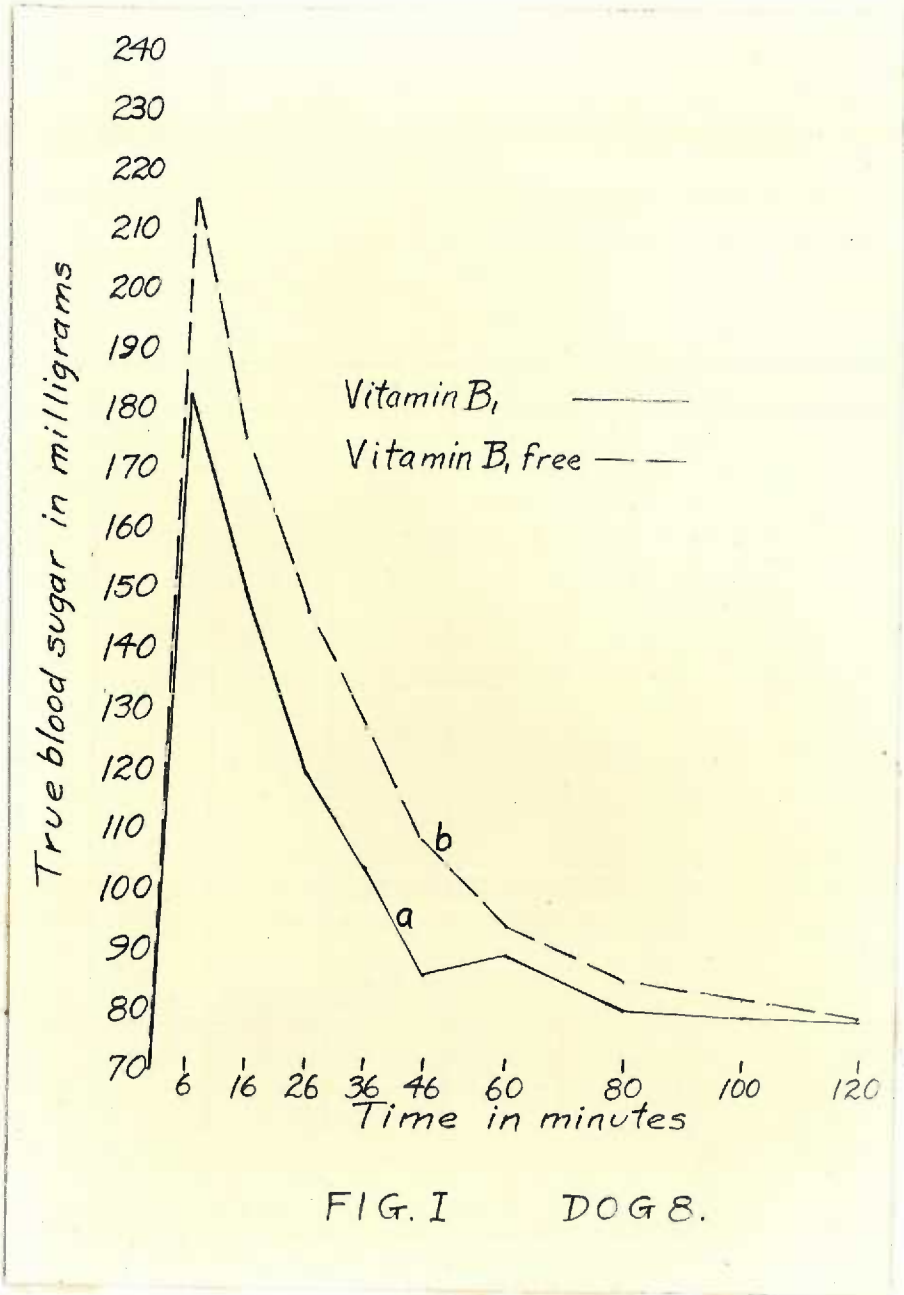

FIG. I DOG 8.

Fig. 1, Dog 8. Curve "a" is constructed from the average of two intravenous tolerance tests while the animal was on a complete diet. Curve "b" is similarly constructed from four tests while on vitamin B free diet.

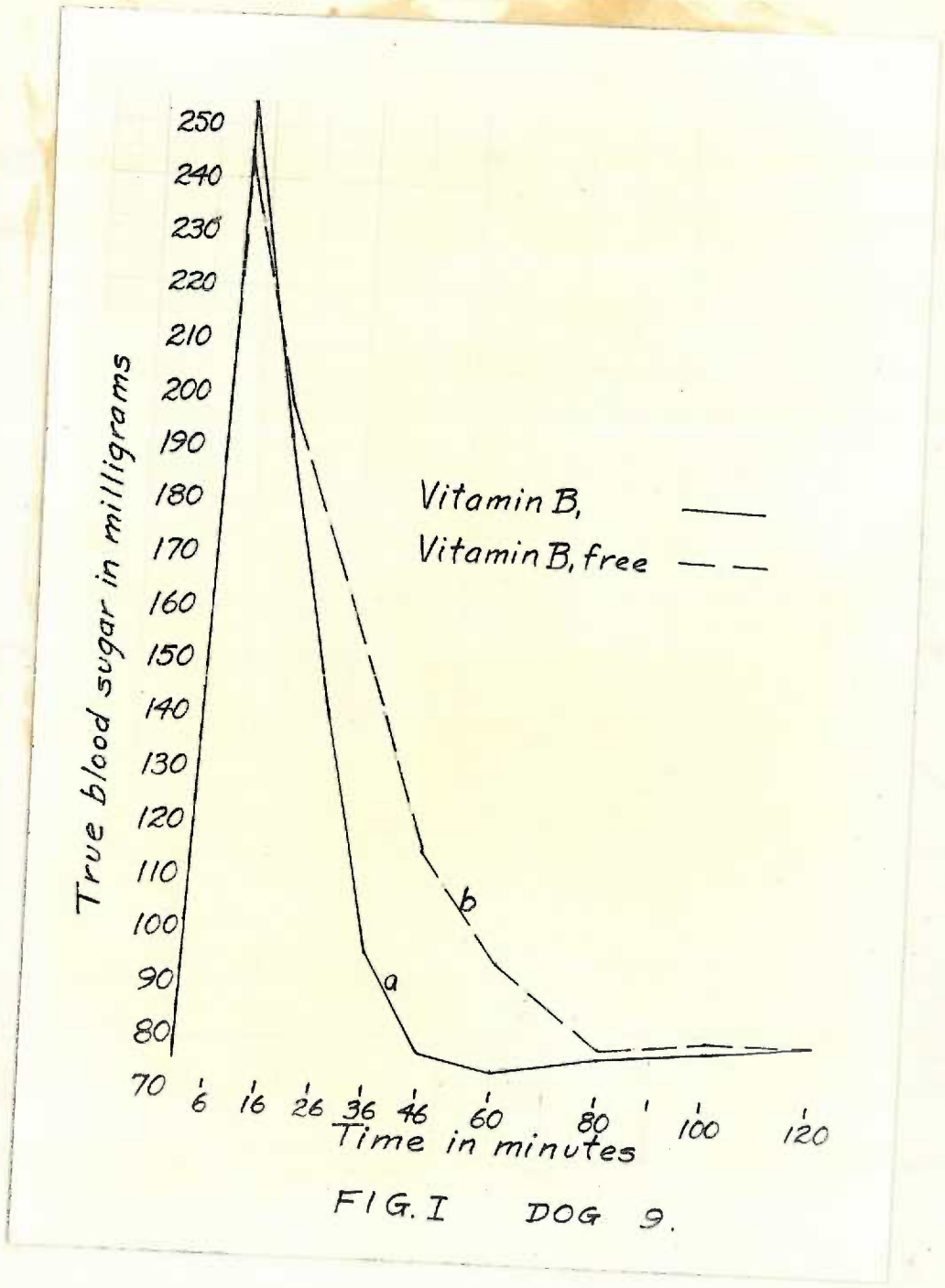

FIG. I DOG 9.

Fig. 1. Dog 9. Curve "a" constructed from average of two intravenous tolerance tests. Normal diet. Curve "b" similarly constructed from four tests while on B free diet.

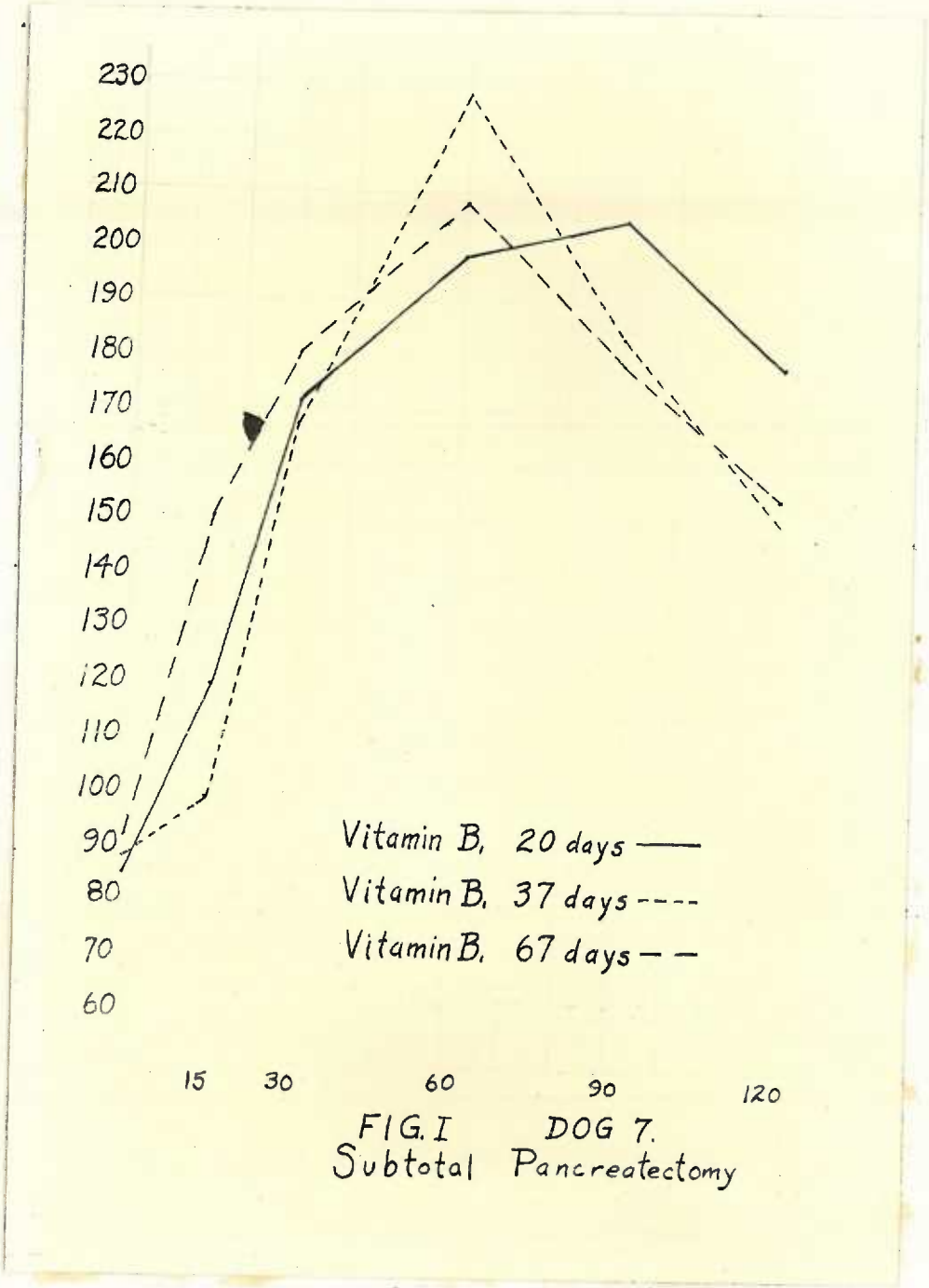

Fig. 1, Dog 7. Subtotal pancreatectomy. Curves representing tolerance tests while the animal was receiving the standard diet and two pulvules of vitamin B daily for twenty, thirty-seven and sixty-seven days.

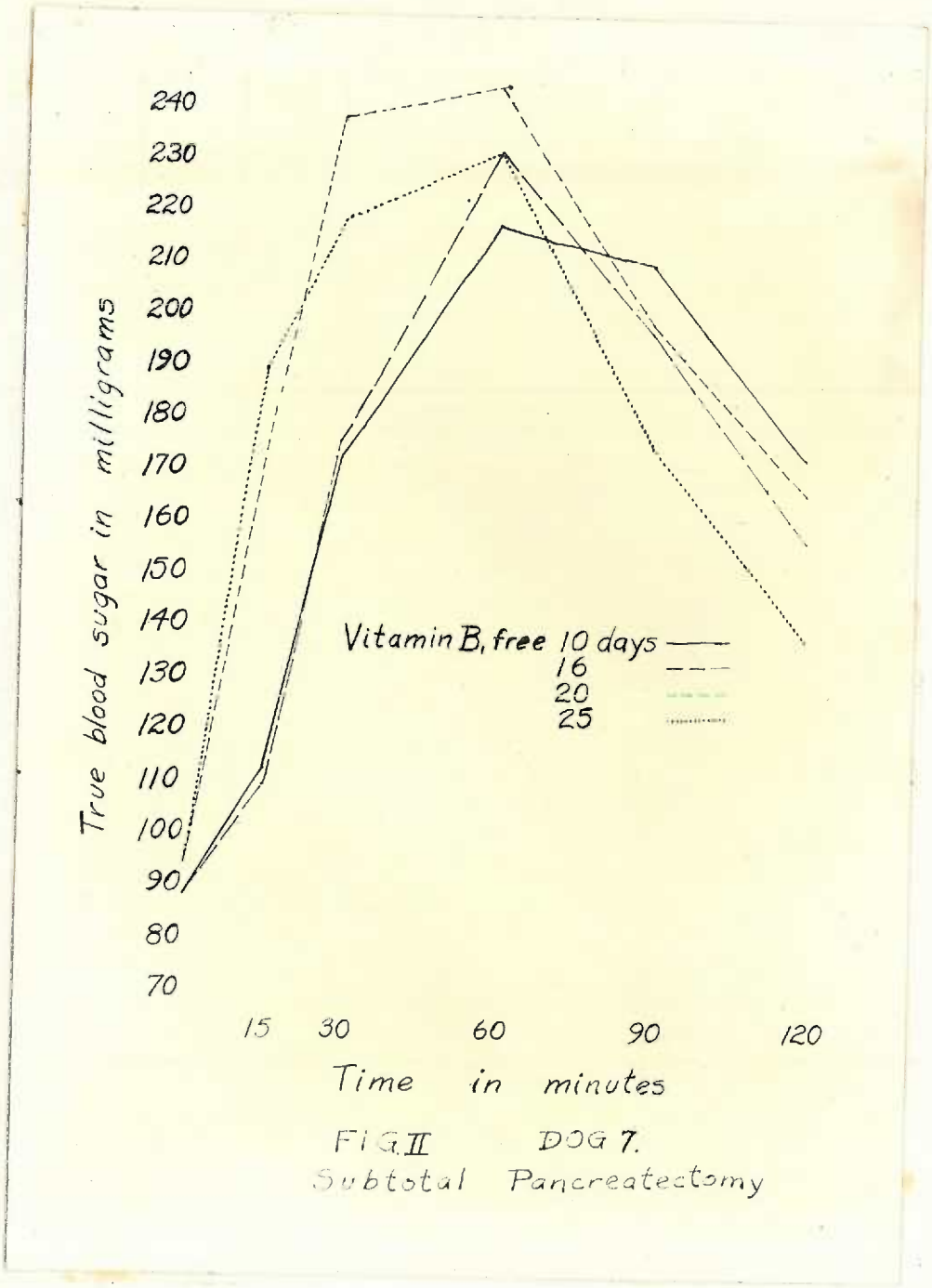

Fig. 2. Dog 7. Subtotal pancreatectomy. Curves from tolerance tests taken ten, sixteen, twenty and twenty-five days after vitamin B was withheld from the diet.

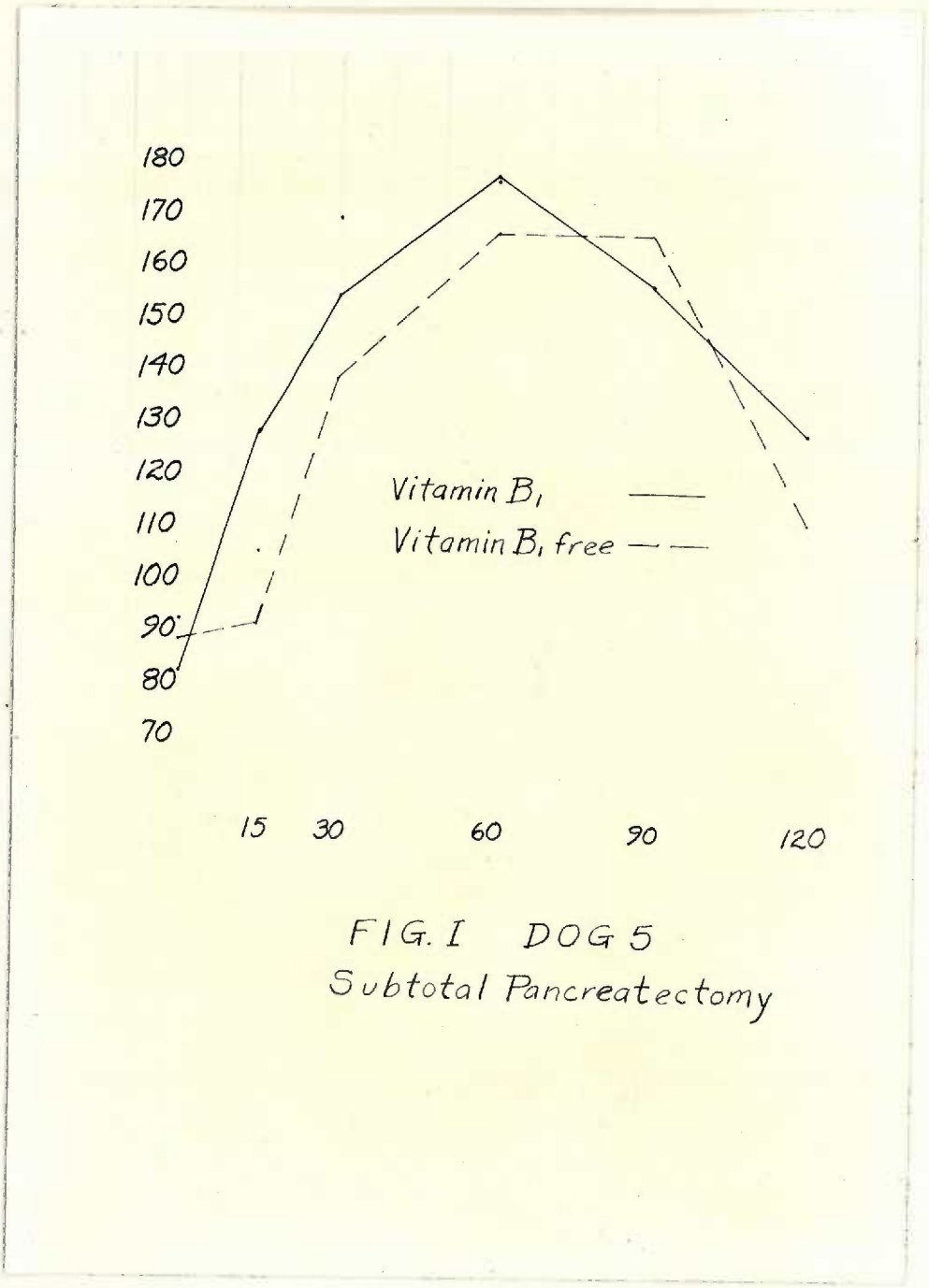

FIG. I DOG 5
Subtotal Pancreatectomy

Fig. 1, Dog 5. Subtotal pancreatectomy. The solid line represents a tolerance test while on the standard diet and one pulvule of vitamin B daily. The broken line is constructed from three tests during a sixteen day period of avitaminosis B.

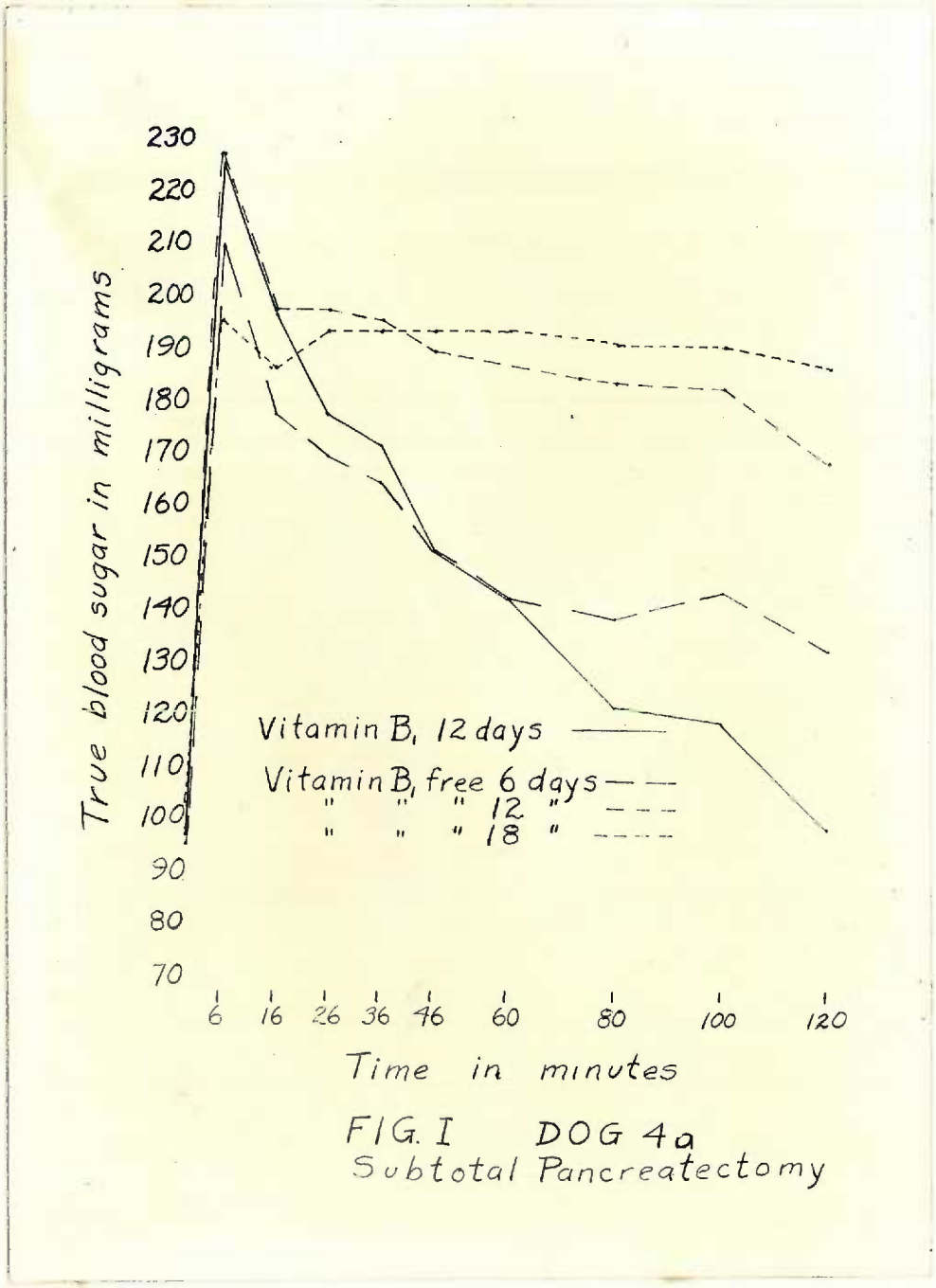

FIG. I DOG 4a
Subtotal Pancreatectomy

Fig. 1, Dog 4a. Subtotal pancreatectomy. Intravenous tolerance tests. The solid line represents a tolerance test when the animal was receiving the standard diet and one pulvule of vitamin B daily for twelve days. The broken lines show the tolerance tests after six, twelve and eighteen days of B deficiency.

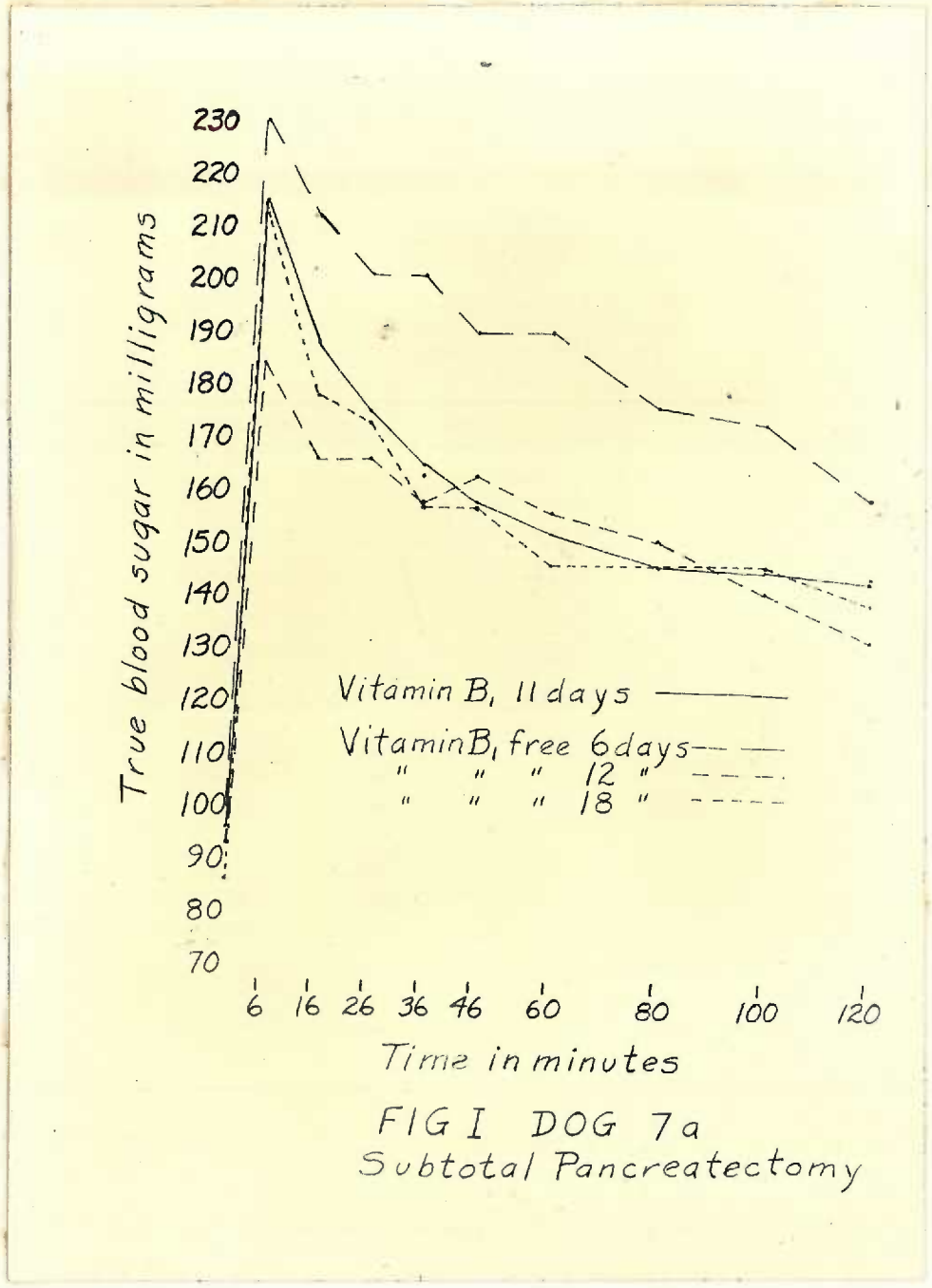

FIG I DOG 7a
Subtotal Pancreatectomy

Fig. 1. Dog 7a. Subtotal pancreatectomy. Intravenous tolerance tests. The solid line represents a tolerance test when the animal was receiving the standard diet and one pulvule of vitamin B daily for eleven days. The broken lines show the tolerance tests after six, twelve and eighteen days of B deficiency.

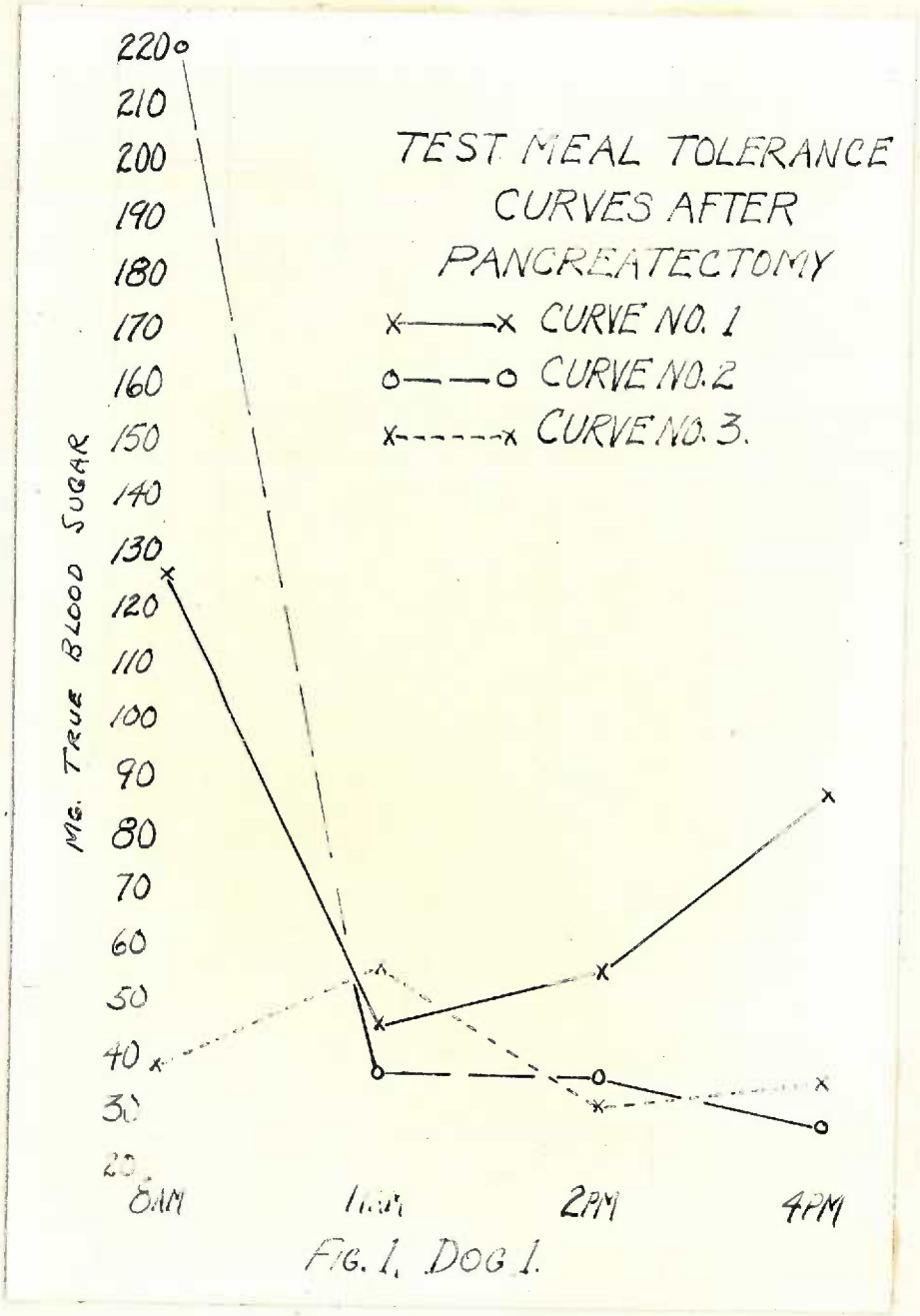

FIG. 1. DOG 1.

Fig. 1, Dog 1. Total pancreatectomy. Test meal tolerance curves. Curve 1, 2 months 16 days after pancreatectomy. Curve 2, 2 months 21 days after pancreatectomy. Curve 3, 3 months 3 days after pancreatectomy.

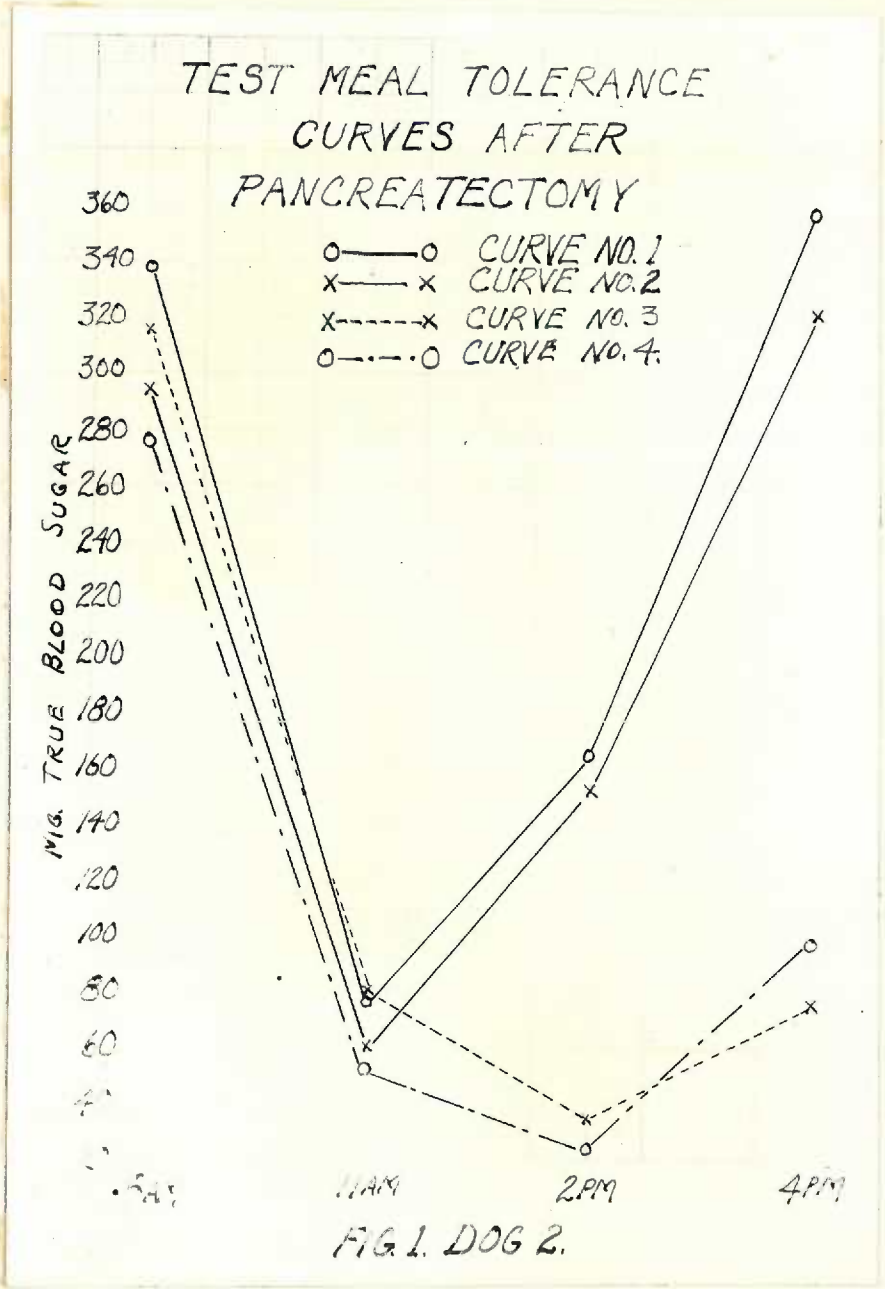

FIG 1. DOG 2.

Fig. 1, Dog 2. Total pancreatectomy. Test meal tolerance curves. Curve 1, 1 month after pancreatectomy and an avitaminosis B for 11 days. Curve 2, 1 month 7 days after pancreatectomy and 5 days after administration of four pulvules of B daily. Curve 3, 1 month 14 days after pancreatectomy and B for 12 days. Curve 4, 2 months after pancreatectomy and an avitaminosis B for 12 days.